

I. Rejection under §112

The Office Action rejects claims 1-14 as indefinite under 35 U.S.C. §112, second paragraph. Applicants respectfully traverse the rejection.

A. The Office Action alleges that claim 1 is drawn to a method for imaging molecules and recites the steps of imaging the array, detecting molecules, aligning discrete regions and determining the amount of signal, but that the claim does not recite steps for imaging molecules.

Amended claim 1 recites "[A] method for imaging an array of discrete reaction sites on the surface of a solid support,..." Claim 1 further recites positive and active steps for imaging the array. In particular, step (i) recites "imaging the array and detecting a signal..." As such, amended claim 1 does not require a defined step for imaging molecules; therefore, claim 1, and claims 3-14 depending from claim 1, are definite. Accordingly, Applicants respectfully request reconsideration and withdrawal of this aspect of the rejection.

B. The Office Action alleges that from the recitation in claim 1, "at a known position with respect to the array," it is unclear where is the "known position," i.e., whether the "known position" is on the array or not. Applicants clarify claim 1 and replace "with respect to" with "on", in step (i), as suggested by the Office Action. As a result, claim 1, and claims 3-14 depending from claim 1, are definite. Accordingly, Applicants respectfully request reconsideration and withdrawal of this aspect of the rejection.

C. The Office Action alleges that the recitation in step (iii) of claim 1, "the amount of detectable signal," lacks proper antecedent basis. Based upon the Office Action's suggestion, Applicants amend claim 1 for clarity. The preamble of amended claim 1 recites "...said molecules being detectably labeled," while step (i) recites "...detecting a signal representing a first molecule..." As a result, "the amount of detectable signal" in step (iii) contains proper antecedent basis; consequently, claim 1, and claims 3-14 depending from claim 1, satisfy the

requirements of 35 U.S.C. §112, second paragraph. Accordingly, Applicants respectfully request reconsideration and withdrawal of this aspect of the rejection.

D. The Office Action alleges that the recitation in claim 14 "the image generated in step (i)" lacks proper antecedent basis. Amended claim 14, recites "the signal detected in step (i)" and as such, has antecedent support from the recitation in step (i) of claim 1 "detecting a signal." Accordingly, claim 14 is definite and Applicants respectfully request reconsideration and withdrawal of this aspect of the rejection.

II. Rejection under §102

A. Noblett

The Office Action rejects claim 1, 2, and 4-10 under 35 U.S.C. 102(e) over U.S. Patent No. 6,362,004 to Noblett ("Noblett"). Applicants respectfully traverse the rejection.

Claim 1 is drawn to a method for imaging arrays of discrete reaction sites located on the surface of a solid support that includes detecting a signal representing a first molecule located on the solid support at a known position on the array, wherein detection of the first molecule is carried out by aligning a first inspection window within a region of the support that includes the first molecule and searching within the window to detect the first molecule. Noblett does not disclose such a method.

Noblett describes a scanning analysis system that utilizes a fiducial mark on a microarray substrate for positioning and aligning the substrate. The fiducial mark allegedly improves the placement of the reaction sites on the microarray. (Col. 6, lines 29-34). More specifically, the fiducial mark is used during the microarray manufacturing process to determine the relative coordinates of the reaction sites positioned on the array. (Col. 6, lines 49-63). In Noblett, the fiducial mark is not within the actual array of reaction sites. As illustrated in Figures 2, 6 and 7, Noblett positions the fiducial mark at a separate and distinct location away from the array. The Noblett manufacturing process additionally requires

spotting software to map the coordinates of the reaction sites relative to the fiducial mark. (Col. 6, lines 46-48 and lines 61-63).

In contrast to Noblett, claim 1 is drawn to a method of detecting signals on a substrate and not a manufacturing process. During signal analysis, the claimed method utilizes a signal representing a first molecule (i.e., the reference molecule) to further align the inspection windows in registration with the discrete reaction sites. The claimed method utilizes the reference molecule to define a fixed location for subsequent alignment of further inspection windows. Once the reference molecule's position has been identified, the analyte inspection windows may be positioned with respect to it, to allow imaging of the reaction sites on the array. Unlike Noblett, the claimed method does not require prior knowledge of the relative position between the reference molecule and the other molecules of the array. As a result, the claimed method is independent of the manufacturing process used to spot the reaction sites on the array. In addition, unlike Noblett, the reference molecule in claim 1 is located "at a known position on the array."

For at least the above reasons, Norbett does not teach or suggest the method of claim 1; thus claim 1 is not anticipated by Norbett. Claims 3-14 depend from claim 1 and also are not anticipated by Norbett. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

B. Juncosa

The Office Action rejects claims 1-12 under 35 U.S.C. 102(e) over U.S. Patent No. 6,309,601 B1 to Juncosa et al. ("Juncosa"). Applicants respectfully traverse the rejection.

Juncosa does not disclose the method of claim 1. Juncosa describes a scanning optical detection system that requires knowledge of the relative coordinates of each microlocation during the detection steps. Juncosa fails to teach or suggest an image processing technique with a grid overlay, positioned relative to a known reference molecule.

Juncosa instead describes a method that relies on a complete scan of the whole solid support surface. (Fig. 6a and Col. 10, line 41 to Col. 11, line 10). Any reference molecule that may be present in the Juncosa system is not used to align further inspection windows.

Juncosa does not disclose the method of instant claim 1 that utilizes the reference molecule to align "inspection windows in registration with the discrete reaction sites" and thus, does not anticipate claim 1. Claims 3-12 depend from claim 1 and also are not anticipated by Juncosa. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

III. Rejection under §103

The Office Action rejects claims 12-14 under 35 U.S.C. 103(a) over Juncosa in view of U.S. Patent No. 5,578,832 to Trulson et al. ("Trulson"). Applicants respectfully traverse the rejection.

Dependent claim 12 recites an imaging method that features a solid support of ceramic, silicon or glass. The Office Action alleges that Juncosa teaches a method of imaging molecules on an array including a solid support, but admits that Juncosa does not disclose a solid support composed of ceramic, silicon or glass. The Office Action alleges that Trulson teaches a similar method of imaging molecules on a solid support of glass, silicon or ceramic. The Office Action concludes that it would have been obvious to one of ordinary skill in the art to apply the glass, silicon or ceramic support of Trulson to the support of Juncosa. Applicants respectfully disagree with this conclusion.

As stated above, Juncosa does not disclose the method of claim 1. Juncosa does not teach or suggest an imaging method that utilizes a reference molecule to align inspection windows in registration with the discrete reaction sites. Trulson also does not teach or suggest such an imaging method and, therefore, Trulson does not overcome the deficiencies of Juncosa.

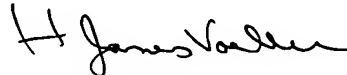
Accordingly, Juncosa and Trulson, either alone or in combination, would not have rendered obvious the imaging method of claim 12. Likewise, the references would not have rendered obvious dependent claims 13 and 14. Applicants respectfully request reconsideration and withdrawal of the rejection.

IV. Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully submit that this application is in condition for allowance. Favorable consideration and prompt allowance are earnestly solicited.

Should the Examiner believe that anything further is desirable in order to place this application in better condition for allowance, the Examiner is requested to contact Applicants' representative at the telephone number listed below.

Respectfully submitted,



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Attachments:
Appendix
Petition for Extension of Time

JAO:HJV/mmc

Date: December 9, 2002

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<p>DEPOSIT ACCOUNT USE AUTHORIZATION Please grant any extension necessary for entry; Charge any fee due to our Deposit Account No. 15-0461</p>
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APPENDIX

Changes to Claims:

Claim 2 is canceled.

The following is a marked-up version of the amended claim(s):

1. (Amended) A method for imaging ~~molecules contained in~~ an array of discrete reaction sites on the surface of a solid support, to detect the presence of molecules on the array, said molecules being detectably labelled, comprising:
 - (i) imaging the array and detecting a signal representing a first molecule located on the solid support at a known position ~~with respect to~~ on the array;
 - (ii) by reference to the first molecule, aligning inspection windows in registration with the discrete reaction sites; and
 - (iii) determining the amount of detectable signal in each window, to thereby detect the presence of the molecules, wherein detection of the first molecule is carried out by aligning a first inspection window within a region of the support that includes the first molecule and searching within the window to detect the first molecule.
3. (Amended) A method according to claim 21, wherein the first inspection window defines a two-dimensional array of pixels and searching is carried out by scanning diagonally the array of pixels and determining values for the pixels.
4. (Twice Amended) A method according to claim-~~2~~ 1, wherein, after detecting the first molecule, the first inspection window is repositioned or enlarged so that one or more of the discrete reaction sites is also located within the window, detecting the one or more sites and, by reference to the first molecule and the one or more sites, aligning a further inspection window in registration with each reaction site of the array.

14. (Twice Amended) A method according to claim 1, wherein the ~~image-~~
~~generated~~signal detected in step (i) must be above a pre-defined value in order to proceed
with steps (ii) and (iii).